



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,859	09/06/2001	Bronwyn Jean Battersby	NMICS-30355	4713
72960	7590	01/13/2009		
Casimir Jones, S.C. 440 Science Drive Suite 203 Madison, WI 53711			EXAMINER WESSENDORF, TERESA D	
			ART UNIT	PAPER NUMBER
			1639	
			MAIL DATE	DELIVERY MODE
			01/13/2009 PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

09/856,859

Applicant(s)

BATTERSBY ET AL.

Examiner

TERESA WESSENDORF

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15, 17-29, 63, 65 and 66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15, 17-29, 63, 65 and 66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/15/08 has been entered.

Election/Restrictions

Applicant's election of species, light emanating feature in the reply filed on 9/22/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants state that claims 17 and 19 are amended to remove reference to non-elected species, reserving the right to restore these claims in the event that a generic claim is allowed. As noted by the Examiner Claim 15 is generic. Species 1 reads on Claims 15, 17-29, 63, 65, and 66.

Status of the Claims

Claims 15, 17-29, 63 and 65-66 are pending and examined on the merits.

Withdrawn Objections/Rejections

IN view of applicants' amendments to the claims and arguments the 35 USC 102 rejection over Natan is withdrawn.

Claim Objections

Claims 19 and 21 are objected to because of the following informalities: "wherein the" in each instance are recited twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 17-29, 63 and 65-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 "integrally associated" is unclear in the manner that the different features are considered

associated integrally to the carrier, especially in the absence of positive definition or support in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(d) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly

or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 15, 17-21, 23-25, 28-2963 and 63-66 are rejected under 35 U.S.C. 102 (b) as being anticipated by Egner et al (Chem. Commun., 1997).

Egner discloses at e.g., page 735, col. 1, a covalently dye beads for combinatorial synthesis of compounds tagged with fluorescence. The dye were covalently coupled by amide bond (claim 29) to Tentagel S-NH₂ beads (130 μ m). The fluorescence technique was extended by the use of a laser system. The Tentagel beads were labeled with florescein and erythrosin. See also Fig. 1 and Fig. 2. and Fig. 4 at page 736. Egner discloses at page 736 col. 2, that the use of colored and fluorescent beads has the potential to simplify the identification of library members for single bead screening application. Please see also the footnotes which teach the excitation of fluorescence by laser beam (claim 19).

Accordingly, the specific carrier of Egner fully meets the claimed plurality of carriers with at least two detectable features.

Claims 15, 17-21, 24 and 65 are rejected under 35
U.S.C. 102(e) as being anticipated by Lawandy (USP
2003/0142713).

Lawandy discloses throughout the patent at the following
e.g., paragraphs:

[0008] A structure that includes a **core or other substrate, at least one and preferably a plurality of optical gain** medium films disposed about said core for providing a **plurality of characteristic emission wavelengths**. The structure may further include a functionalized support suitable for the synthesis therein or thereon of a chemical compound. Various structure geometries are disclosed, such as disks and spheres...(Reads on claims 15, 17-21)

[0011] Also disclosed is a bead of a type that includes a functionalized support (a growth matrix suitable for use in at least a combinatorial chemistry application), and that further includes a gain medium coupled to a structure that supports the creation of at least one mode for electromagnetic radiation, and/or which has a dimension or length in one or more directions for producing and supporting amplified spontaneous emission (ASE). The structure can have boundaries that impart an overall geometry to the structure that, in combination with at least one material property of the structure, supports an enhancement of electromagnetic radiation emitted from the gain medium by favoring the creation of at least one mode that enhances an emission of electromagnetic radiation within a narrow band of wavelengths. Information is encoded into the bead using only wavelength encoding, or by using both wavelength encoding and signal level encoding. The information may be encoded using one of a single level encoding or multi-level encoding

[0029] FIG. 19 illustrates a substrate having embedded fibers or threads that emit narrow-band light, when excited by an optical source such as a laser, containing one or more characteristic wavelengths.

Art Unit: 1639

[0069] ...[a] population of beads, where each bead includes a functionalized support and a means for optically encoding bead identification information. ... [a] sensor that is responsive to a desired bead activity for identifying a location of one or more beads of interest within the population of beads.....(All of the above reads on claims 15, 17-21, 25).

[0080] FIG. 17 is a top view of the substrate or wafer 110, such as that shown in FIG. 14, which contains a plurality of regions each defining one of the lasing bead structures, and further shows wavelength calibration and slicing of the wafer into individual lasing bead structures 110a. In this case the particular wavelength signature of each bead structure 110a can be readout by illuminating with a suitable excitation source (e.g., a laser), detecting the emitted wavelengths, and then cataloging and storing... the wavelength signature. The slicing of the wafer into individual laser bead structures can be accomplished by, for example, scribing and breaking, mechanical sawing, or by laser cutting[0100] For the case where the coating 232 is applied, the coating can be selected to be or contain a fluorescent material. In this case the coating 232 can be excited with a UV source to provide the broadband emission.

[0074] FIG. 14 is a block diagram of a lasing bead structure fabrication print step, wherein an N 'color' head 102 is controlled by a head controller 104 and a computer 106. A substrate 110, such as a one meter by one meter polymeric (e.g., a cross-linked polystyrene) or glass substrate (or other suitable material), is placed on an X-Y stage 108 beneath the head 102. The head 102 includes a capillary dispenser 102a, preferably capable of movement along a Z-axis, for controllably placing or printing "dots" of selected gain medium material, such as one or more of those listed previously, onto a surface region of the substrate 110. Each dot can be considered to be a micro-laser capable of a laser-like emission at a predetermined wavelength or 'color'. The illustrated embodiment shows three dots for emitting at $\lambda_{sub.1}$, $\lambda_{sub.2}$, and $\lambda_{sub.3}$. Each region would thus contain a plurality of dots and would be capable of emitting with a plurality of distinguishable wavelengths.

[0134] This invention further teaches a bead structure comprising an optical gain medium and a structure having boundaries that impart an overall geometry to the structure that, in combination with at least one material property of the structure, supports an enhancement of electromagnetic radiation emitted from the gain medium for favoring the creation of at least one mode that enhances an emission of electromagnetic radiation within a narrow band of wavelengths. Suitable, but not limiting, shapes for the structure comprise elongated, generally cylindrical shapes such as filaments, a sphere shape, a partial-sphere shape, a toroidal shape, a cubical and other polyhedral shape, and a disk shape. (Claim 65).

Accordingly, the specific carrier of Lawandy fully meets the claimed plurality of carriers with at least two detectable features.

Claims 15, 17-29, 63 and 65-66 are rejected under 35 U.S.C. 102(a) as being anticipated by Garman et al (WO 9847838).

Garman discloses throughout the patent at e.g., page 5, lines 11-15 synthetic particles as beads, for example polymer beads or glasses that exhibit features that allow them to be distinguished optically. These features may be intrinsic to the bead that is, conventional beads used for compounds synthesis may be distinguished on the basis of size, shape, surface features or other feature or combination of features. Garman discloses at e.g., page 6, line 5 up to page 7, 10 that an optically distinguishable features mean micro particles, specks which makes each bead distinguishable from the others . The beads are preferably spherical suitable for library synthesis.

The size is 100-300 micron but other sizes depend on the number of compounds to be synthesized, scale and other factors. The optically distinguishable features are microparticles which can be in the range of 0.5-40 micron. The microparticles are incorporated into the bead. Page 9, Fig. 1 refers to a G-NH₂ bead (reads on claim 29).

Accordingly, the specific carrier of Garman fully meets the claimed plurality of carriers with at least two detectable features.

Claims 15-19, 22-25, 28-29 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamashita et al (WO 95/32425).

Yamashita discloses throughout the patent at e.g., beads which is a solid support material capable of providing a base for combinatorial synthesis such as Tentagel of 10-100 micron particles. The beads has a tag which is an encoding characteristic of a bead or groups of beads capable of being sorted by flow cytometry, such as differences in size, fluorescent marker , a fluorescent label identifier. The fluorescent label identifier is a coding label attached to a bead or group of bead either by adding ratios of a flourophor or by adding multiple, preferably two different flourophores of

varying ratios. A combinatorial library containing tagged beads is shown at pages 6-9. See also page 17, lines 11-25., and page 19, Scheme 3. The multiple flourophors and linkers are disclosed at page 20, lines 5-15. See also, page 30, lines 9-16, Procedures D and E.

Accordingly, the specific carrier of Yamashita fully meets the claimed plurality of carriers with at least two detectable features.

Claims 15, 17-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Seul et al (USP 7083914).

Seul et al discloses throughout the patent at e.g., col. 5, line 29 up to col. 6, line 56:

...[c]olor codes for the purpose of uniquely labeling members of a group of beads or equivalent objects ("beads") to preserve the chemical identity of the beads and thus the identity of bead-coupled chemical compounds. These color codes are based on a set of encoding fluorophores of distinguishable wavelengths, excited-state lifetimes and levels of intensity, the latter controlled by adjusting the abundances of dyes.

Binary and extended binary color codes offer large coding capacity and represent a general strategy to encode multi-step reaction histories such as those encountered in divide-couple-recombine (DCR) synthesis strategies for combinatorial chemical libraries.

Simple and extended simple color codes offer an efficient strategy to encode a smaller set of distinct chemistries that are typical of panels displaying multiple targets or probes in biochemical assays including multi-agent

diagnostic and environmental tests and other biochemical assays.

All color codes can be augmented by varying distinguishable features of beads such as shape and size or other suitable physico-chemical parameter associated with bead cores such as polarizability.
Please see also all the drawing Figures.

Accordingly, the specific carrier of Seul et al fully meets the claimed plurality of carriers with at least two detectable features.

Claims 15, 17-29, 63 and 65-66 are rejected under 35 U.S.C. 102(e) as being anticipated by Kauvar et al (USP 6642062).

Kauvar discloses throughout the patent at e.g., col. 2, line 48 up to col. 5, lines 63:

...[a] label which comprises a particulate support to which is bound at least two signal generating moieties, which moieties generate signals that can be distinguished in situ, such as light of different wavelengths. These labels are distinguishable by any instrumentation which contains separate means for detection for each of the at least two in situ signals generated.

... [a] collection of labels wherein the ratio of the moieties differs from label to label in the collection. Typically, this collection of labels provides identifiable members that number at least twenty... Thus, if the reliability of detection of each color is plus or minus 10 percent, 10 gray labels exist for each signal and therefore 100 hues can be distinguished when two signal generating moieties are included in each label.
This instrumentation provides fluorescence excitation and capacity for detection of three separate wavelengths of light.....Such beads are available commercially in several

Art Unit: 1639

different colors of fluorophores with high uniformity in size and fluorophore doping levels from Flow Cytometry Standards Corp....among others.

...[t]he number of reagents that can be separately detected under these conditions by systematic and precise doping of particulate supports with signal generating moieties, typically fluorophores, of different colors corresponding to the CCD detectors employed, at specified ratios. Particles with different ratios of the fluorophores generate different detection signals in this system. Because the ratios of the fluorophores can be varied at will, up to a point where a forced proximity of the dyes leads to quenching, many different "hues" can be generated in a collection of labeled particles, each particle type having a unique ratio and/or amount of color generating moieties.

As used herein, the term "label" is generally used to describe a particulate support to which has been bound an appropriate array of signal generating moieties. The signal-generating moieties must be such that the signals are detected in situ on the particulate support. Thus, it is unnecessary to detach the signal-generating moieties from the support in order to ascertain their ratio. Their ratio is read directly by means of the "hue" of the label. Color is a preferred signal. The labels....contain at least two, and preferably at least three, distinguishable signal generating moieties.

As visible light is a particularly convenient way to generate a particular "hue,"... However, other signal generating moieties can be employed or an indirect method to generate visible light may be used. In addition, heavy atom clusters of different materials, for example colloidal gold dots versus ferrite rods offer different scattering characteristics with respect to electron microscope beams. The preferred "color generating" moieties are typically fluorophores, but they can also generate a characteristic wavelength either by reflectance (simple dyes) or by emission (fluorophores or de novo light-generating compounds such as a luciferase or other chemiluminescent system). A number of chemiluminescent systems are known in the art such as horseradish peroxidase-based generation of chemiluminescent products.... In addition to fluorescent

Art Unit: 1639

dyes, phosphorescent materials may also be employed which adds the advantage that time resolved fluorescence distinguishes signals that would be equivalent averaged over a longer detection period.

The supporting particles are typically 0.1-1 .mu.m in diameter and are preferably latex. However, smaller particles may also be used. Generally, 50 nm (0.05 .mu.m) is considered an approximate minimum; it has been possible in some contexts to use particles as large as 5 .mu.m, although this is not preferred. The use of larger particles results in lower diffusion rates and thus, effectively, less efficient and less vivid labeling. A preferred range is 100-500, preferably 100-300, and more preferably 100-200 nm diameter particles. The particulate supports are generally spherical, and the microscopic techniques employed can distinguish spherical shapes from other general outlines. **Silica** gel particles may also be used. Any particulate that has suitable physical properties (does not spontaneously aggregate, adhere, or otherwise fail to behave as an independent particle) and which can be suitably derivatized with the color generating moieties and with the test reagent may be used.

The construction of the particle itself affects the hue detected. In addition to differences attributed to the size of the particle, as indicated above, the shape will determine the nature of the signal. Shapes can vary along the continuum of sphere to oval to rod to string, for example. Star shapes or other arbitrarily shaped particles can be created by x-ray lithography so as to have a distinctive point spread function.

Accordingly, the specific carrier of Kauvar fully meets the claimed plurality of carriers with at least two detectable features.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15, 17-29, 63 and 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over anyone of the cited references above e.g., Egner et al, Lawandy, Garman, Yamashita ,Seul or , Kauvar (hereinafter the primary references) in view of either kris et al (USP 6238869) or Kimura et al (USP 6228480).

Each of the primary references is discussed above. Each of the primary references does not disclose the carrier as a silica microparticle as recited in e.g., claim 27.

Kris discloses throughout the patent at e.g., col. 5, lines 3-30:

The surface (usually a solid) can be any of a variety of organic or inorganic materials or combinations thereof, including,...plastics such as polypropylene or polystyrene; ceramic; silicon; (fused) silica, quartz or glass microscope slide or a glass cover slip;..Substrates that are transparent to light are useful when the method of performing an assay involves optical detection...The shape of the surface is not critical. It can, for example, be a flat surface such as a square, rectangle, or circle; a

curved surface; or a three dimensional surface such as a bead, particle, strand, precipitate, tube, sphere; etc.

Kimura et al discloses at e.g., col. 4, lines 15-45:

If the adhesive layer is composed of a resin that contains colloidal silica, it is preferable if the diameter of colloidal silica particles is 10 nm or less.....As a method to introduce such colloidal silica into the resin, it is known that a method to mix a resin solution with a colloidal silica solution, then apply it and subsequently dry it to form an adhesive layer is the easiest, however, a method to form an adhesive layer by allowing a resin to polymerization while dispersing colloidal silica in the resin and then to apply the synthesized resin and dry it, is also acceptable. It is also possible to use colloidal silica after treating it with a silane coupler for improving adhesive property and dispersibility of colloidal silica and a resin.

As examples for a resin whereto colloidal silica is introduced, acryl resin, acryl-silicon resin, epoxy-silicon resin, silicon-modified resin, urethane resin, epoxy resin, polyester resin, alkyd resin, etc. are given, however, silicon-modified resins including acryl-silicon resin and epoxy-silicon resin, are the most suitable one in term of durability.

As the colloidal silica, any silica sol, which is produced either by subjecting sodium silicate solution to cation exchange or by subjecting silicon alkoxide to hydrolysis, can be used.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use silica microparticle as the carrier in anyone of the primary references as taught by either Kris or Kimura. One would have a reasonable expectation or predictable result since as Kimura or Kris teaches that silica or a large number of carriers has been

successfully employed in the art for combinatorial library synthesis of compounds.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. USP 6268222 teaches microparticles attached to nanoparticles labeled with fluorescent dye. E.g., of the carrier is silica.
2. USP 6416949 discloses a method of synthesizing diverse collections of oligomers.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 09/856,859
Art Unit: 1639

Page 17

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639